REMARKS

Claims 1-3 and 5-6 are pending after entry of the amendments set forth herein. Claims 4 and 7 are canceled without prejudice. Claims 1-3 and 5-6 are amended. Support for these amendments is found in the specification as described below. No new matter is added.

Support for the specific asthma/atopy systems may be found in the specification, where Example 1, paragraphs [51]-[53], discloses primary human umbilical vein endothelial cells (HUVEC) in the presence of IL-4 and histamine with at least three different cellular parameters selected from CD55, VCAM-1, P-selectin, Eotaxin-3, MCP-1, VEGF receptor 2 and uPAR (CD87).

Example 2, paragraphs [55]-[59] discloses HUVEC and T cells in the presence of IL-2 and superantigen with at least three different parameters selected from IFN-γ, TNF-alpha, IL-2, IL-4, IL-5, IL-8, IL10, IL-13, LT-alpha, CCR4, CCR5, CXCR3, IL-4Ralpha, CD11c, CD38, CD40, CD69, E-Selectin, Eotaxin-3, CD106, CD134, CD150, CD137, CD69, CD200, B7-H1, B7-H2, MIG and CD87.

Example 3, paragraphs [60]-[66] discloses Human neonatal fibroblasts (HDFn) in the presence of TNF, IL-1, IFN and TGFβ with at least three different parameters selected from ICAM, VCAM, CD40, CD90, IP-10, MCP-1, Collagen I, Mig, m-CSF, TIMP-2, PAI-I, and IL-8; HDFn in the presence of TGFβ with at least three different parameters selected from CD90, Collagen I, Collagen III, HLA-DR, PAI-I, and VCAM; and HDFn in the presence of TGFβ, IL-4, and IL-13 with at least three different parameters selected from CD40, CD90, Collagen I, Collagen III, MMP-1, MMP-13, Eotaxin 3, m-CSF, ICAM, TIMP-2; PAI-I, and VCAM.

Example 4, paragraphs [60]-[62] discloses primary human umbilical artery smooth muscle cells in the presence of IL-4 and histamine with at least three different parameters selected from VCAM, CD40, HLA-DR, ICAM, IL-8, MCP-1, M-CSF, MIG, Thrombomodulin, and uPAR; and primary human umbilical artery smooth muscle cells in the presence of IL-1, TNF-α and IFNγ with at least three different parameters selected from VCAM, CD40, HLA-DR, ICAM, IL-8, MCP-1, M-CSF, MIG, Thrombomodulin, and uPAR.

Example 5, paragraphs [67]-[69] discloses human bronchial epithelial cells in the presence of IL-1β, TNFα and IFN-γ with at least three different parameters selected from ICAM-1, IL-1a, IP-10, TGF-β, MIG, HLA-DR, PAI-1, I-TAC, MMP-1, MMP-9, CD87 and Keratin 8/18; and human bronchial epithelial cells in the presence of IL-4, IL-13 and TNFα with at least three

different parameters selected from Eotaxin-3, ICAM-1, IL-1a, IL-8, TGF-β, PAI-1, MMP-9, uPA and Keratin 8/18.

Support for the amending language "characterization of a biologically active agent according to its mechanism of action in an asthma/atopy context" may be found in the description of the field of the invention, paragraph [01].

Support for the amending language "measuring changes in parameters as a result of introduction of said agent in said at least three different cellular parameter readouts" may be found in the specification at paragraph [31] and [42]. Paragraph [32] references the desirability of measuring at least three parameters.

Claims 1-7 have been rejected under 35 U.S.C. 101. The Office Action asserts that the claimed invention is directed to nonstatutory subject matter because the claims are drawn to methods of comparing data profiles. These methods are stated to be nonstatutory because "The methods do not require a particular machine or apparatus. They do not perform a transformation of matter. Further, the claims lack a practical application of the method and the result of the method. The resulting sets of the claims are not clearly useful. No tangible output is set forth." Applicants respectfully disagree, and submit that the independent claims to conform to the most recent Federal Circuit case law on the patentability of screening methods under 35 U.S.C. § 101.

As amended, the pending claims recite, in shortened form, a method for characterization of a biologically active agent according to its effect on allergic or atopic conditions, by contacting the agent with an asthma/atopy context system, measuring changes as a result of introduction of said agent in said at least three different parameters; deriving a biological dataset from changes in parameter readouts, wherein the biological dataset comprises control data from a system lacking the biologically active agent; and comparing the biological dataset to a reference biological dataset to characterize the agent's effect on allergic or atopic conditions.

As explained by the Federal Circuit in *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*, No. 08-1403 (Fed. Cir. Sept. 16, 2009), the amended claims are patentable subject matter under 35 U.S.C. § 101. First, the amended claims meet the transformation prong of *In re Bilski,* (2007-1130 (Fed. Cir. 2008)):

> The determining step ... is ... transformative and central to the claimed methods. Determining the levels of 6-TG or 6-MMP in a subject necessarily involves a transformation, for those levels cannot be determined by mere inspection. Some form of manipulation, such as ... high pressure liquid chromatography ... is necessary to extract the metabolites from a bodily sample and determine their concentration. As stated by

> Prometheus's expert, 'at the end of the process, the human blood sample is no longer human blood; human tissue is no longer human tissue.' ... That is clearly a transformation.

Prometheus Labs, No. 08-1403, pages 16-17. Because the amended claims determine changes in cellular parameters that result from introduction of a test agent, these claims likewise transform physical subject matter and meet the transformation prong of *In re Bilski*.

The Federal Circuit also explained why the determining step is not merely a necessary data-gathering step or insignificant post-solution activity. Regarding data gathering, the Federal Circuit stated:

> this transformation is central to the purpose of claims, since the determining step ... is what enables possible adjustments to ... drug dosage ... for optimizing efficacy or reducing toxicity during a course of treatment. The determining step, by working a chemical and physical transformation on physical substances, likewise sufficiently confines the patent monopoly, as required by *Bilski*.

Prometheus Labs, No. 08-1403, page 17. Regarding insignificant extra-solution activity, the Federal Circuit stated:

> the ... determining [step is] ... not 'merely' ... 'insignificant extra-solution activity" [it is] part of [a] treatment [regime] for various diseases... As a result, the ... determining [step is] not insignificant extra-solution activity and the claims are therefore not drawn merely to correlations between metabolite levels and toxicity or efficacy.

Prometheus Labs, No. 08-1403, page 19. Like the claims at issue in *Prometheus Labs*, Applicants' amended claims include a determining step, the results and analysis of which are used to classify a candidate agent according to its effect on asthma or atopy. Accordingly, the determining step of Applicants' claims is not mere data gathering or insignificant post-solution activity.

Because Applicants have amended the claims to conform with the scope of subject matter described as patentable by the Federal Circuit under 35 U.S.C. § 101, Applicants submit that the claims as amended recite patentable subject matter.

Claims 1-7 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner has stated that It is unclear what parameters are to be obtained and what the asthma/atopy context system. Applicants have amended the claims to clarify the systems that provide an asthma/atopy context, including specific parameters, cells and factors. The claims further specify that the dataset provides a compilation of parameter changes in test and

control samples, and how the control and reference datasets are obtained. Antecedent support for "candidate agent" has been provided.

Applicants submit that the term "genetic agent" is discussed at length in the specification, for example at paragraph [41], which reads:

> The term "genetic agent" refers to polynucleotides and analogs thereof, which agents are tested in the screening assays of the invention by addition of the genetic agent to a cell. Genetic agents may be used as a factor, e.g. where the agent provides for expression of a factor. Genetic agents may also be screened, in a manner analogous to chemical agents. The introduction of the genetic agent results in an alteration of the total genetic composition of the cell. Genetic agents such as DNA can result in an experimentally introduced change in the genome of a cell, generally through the integration of the sequence into a chromosome. Genetic changes can also be transient, where the exogenous sequence is not integrated but is maintained as an episomal agents. Genetic agents, such as antisense oligonucleotides, can also affect the expression of proteins without changing the cell's genotype, by interfering with the transcription or translation of mRNA. The effect of a genetic agent is to increase or decrease expression of one or more gene products in the cell.

One of skill in the art would readily understand that a genetic agent refers to such polynucleotides and analogs thereof. However, to further prosecution Applicants have amended Claim 2 to recite such specifically.

Similarly, one of skill in the art reading the specification would readily interpret Claim 3, however in order to further prosecution Applicants have amended the claim to recite a drug or polypeptide, as discussed in the specification at paragraph [39].

Claims 5 and 6 have been rewritten to clarify that a plurality of systems selected from the provided list are utilized in Claim 5.

With respect to Claim 6, the Examiner has questioned how to concatenate a data system. Applicants submit that one of skill in the art can readily determine methods of concatenating profiles to perform simultaneous analysis of multiple systems, as set forth at paragraph 31 of the specification.

Should further information be deemed to be required, Applicants submit that paragraph 17 of the specification references co-pending applications that relate to the systems of the invention, including in co-pending U.S. provisional patent application 60/539,447, filed January 26, 2004, which was specifically incorporated by reference. This application is not pending as USSN 10/553,818. Applicants note, in particular, paragraphs 70-71 of the application, which read as follows:

> To allow objective evaluation of the significance of all relationships between compound activities, profile data from all multiple systems may be concatenated; and the multi-system data compared to each other by pairwise Pearson correlation. The relationships

> implied by these correlations may then be visualized by using multidimensional scaling to represent them in two or three dimensions.
>
> In order to accomplish this, multidimensional scaling is used on the original profiles, transforming each one of them into a point in 2D or 3D space. The use of MDS for this operation is preferred because it preserves the relative distance of the nodes. Distances between agents are representative of their similarities and lines are drawn between compounds whose profiles are similar at a level not due to chance.

In view of the above amendments and remarks, withdrawal of the rejection is requested.

Claims 1-7 have rejected under 35 U.S.C. 102(b) as being anticipated by Berg et al. US 6,656,695; by Berg et al. US 2003/017445, by Berg et al. US 2003/0113807, or by Plavec et al. US 7,266,458.

The Office Action states that Berg et al. disclose a method of characterization of agents using the Biomap system of the instant specification, where asthma and atopy context systems are specifically described, e.g. at column 32-35 of the '695 patent.

Applicants respectfully submit that the systems set forth in the present claims are not anticipated by the cited art. The '695 patent teaches, with respect to endothelial cells (HUVEC), that "inflammation in chronic Th2 environments, such as asthma, is characterized by the presence of TNF-α, IL-1 and IL-4, but not IFN-γ" (column 32, lines 45-50). The present claims include one asthma context system utilizing HUVECs, but in the presence of histamine and IL-4; or in the presence of T cells. As such, the HUVEC systems are not taught by the '695 patent.

The '695 patent teaches, with respect to T cells, that "the disease environment in asthma includes IL-1α, IL-4, IL-5, IL-6 and GM-CSF (Miadonna, 1997; Walker, 1994), therefore, an assay combination for asthma will contain one or more of these factors, generally including at least two of the IL factors and GM-CSF" (column 34, lines 13-18). The present claims require a T cell system in combination with HUVEC, IL-2 and superantigen. As such, the T cell system is not taught by the '695 patent.

As noted by the Examiner, the '695 patent teaches the use of mast cells, however such systems are outside of the present claims. Applicants were enable to find a reference to bronchial cells in the '695 patent.

In view of the above amendments and remarks, Applicants respectfully submit that the present claims are not taught by the cited art, U.S. Patent no. 6,656,695.

With respect to US 2003/017445, Applicants respectfully request clarification of the intended reference, as the serial number does not match any of the cited documents.

With respect to Berg et al. US 2003/0113807, the teachings that relate to asthma are as cited for the '695 patent, where HUVEC systems may be found at paragraph [143]; and T cells at paragraph [151]. The teachings of mast cells and bronchial cells are also as described for the '695 patent.

In view of the above amendments and remarks, Applicants respectfully submit that the present claims are not taught by the cited art, US 2003/0113807.

With respect to Plavec et al. US 7,266,458, the teachings that relate to asthma are as cited for the '695 patent, where HUVEC systems may be found at column 27, lines 1-42; T cell systems are discussed at column 29, lines 5-10, and mast cells are discussed at column 30, lines 5-29.

In view of the above amendments and remarks, Applicants respectfully submit that the present claims are not taught by the cited art, US 7,266,458.

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number SEEK-009.

Respectfully submitted,
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Date: March 26, 2010

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